

RECEIVED

MAY 31 2001

TECH CENTER 1600/2900

C1

(c) a fragment of the sequence of SEQ ID NO:1,  
which fragment potentiates cell death; or  
(d) a derivative of (a), (b) or (c).

--41. A polypeptide in accordance with claim 40  
encoding a sequence comprising SEQ ID NO:1.

--42. A polypeptide in accordance with claim 40  
encoding a sequence comprising an analog of SEQ ID NO:1,  
having no more than ten changes in the amino acid sequence of  
SEQ ID NO:1, each said change being a substitution, deletion  
or insertion of a single amino acid, which analog potentiates  
cell death.

--43. A polypeptide in accordance with claim 40  
consisting of a fragment of the sequence of SEQ ID NO:1, which  
fragment potentiates cell death.

--44. A DNA sequence encoding a polypeptide in  
accordance with claim 40.

--45. A DNA sequence encoding a polypeptide in  
accordance with claim 41.

--46. A DNA sequence encoding a polypeptide in  
accordance with claim 42.

--47. A DNA sequence encoding a polypeptide in  
accordance with claim 43.

--48. A DNA sequence in accordance with claim 44,  
consisting essentially of SEQ ID NO:2 or a portion thereof  
encoding a polypeptide which potentiates cell death.--

C2

5 (Amended). A vector comprising a DNA sequence  
according to claim 44.

C3

11 (Amended). A method for producing a polypeptide which directly or indirectly potentiates cell death, which comprises growing a transformed host cell according to claim 8 under conditions suitable for the expression of an expression product, effecting post-translational modification of said expression product, as necessary, for obtaining said polypeptide, and isolating said expressed polypeptide.

C4

12 (Amended). Antibodies or active fragments or derivatives thereof, specific for a polypeptide according to claim 40.

Delete claim 13 and substitute therefor new claim 49 as follows:

C5

--49. A method for the modulation of the effect on cells of the B1 polypeptide of SEQ ID NO:1, comprising treating said cells with a polypeptide in accordance with claim 40, wherein said treating of said cells comprises introducing into said cells said polypeptide in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells.--

C6

14 (Amended). A method according to claim 49, wherein said treating of cells comprises introducing into said cells a DNA sequence encoding said polypeptide in the form of a suitable vector carrying said sequence, said vector being

LAST AVAILABLE COPY

C 6 capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

C 7 15 (Amended). A method according to claim 14, wherein said treating of said cells comprises:

(a) constructing a recombinant animal virus vector carrying a sequence encoding a viral surface protein (ligand that is capable of binding to a specific cell surface receptor on the surface of said cells to be treated and a second sequence encoding said polypeptide; and

(b) infecting said cells with said vector of (a).

C 8 16 (Amended). A method for modulating the effect on cells of the B1 protein of SEQ ID NO:1, comprising treating said cells with antibodies or active fragments or derivatives thereof, according to claim 12, said treating being by application to said cells of a suitable composition containing said antibodies, active fragments or derivatives thereof, wherein when said B1 protein of said cells is exposed on the extracellular surface, said composition is formulated for extracellular application, and when said B1 protein is intracellular, said composition is formulated for intracellular application.

17 (Amended). A method for modulating the effect on cells of the B1 protein of SEQ ID NO:1, comprising treating said cells with an oligonucleotide sequence encoding an antisense sequence of at least part of a mRNA sequence encoding said B1 protein, said oligonucleotide sequence being capable of blocking the expression of said B1 protein.

Delete claim 18 without prejudice and substitute  
therefor new claim 50 as follows:

C9 --50. A method according to claim 17, wherein said  
treating of said cells is by transfection of said cells with a  
recombinant animal virus vector by a process comprising:

(a) constructing a recombinant animal virus vector  
carrying a sequence encoding a viral surface protein (ligand)  
that is capable of binding to a specific cell surface receptor  
on the surface of said cells to be treated, and a second  
sequence comprising said antisense oligonucleotide sequence;  
and

(b) infecting said cells with said vector of (a).--

C10 19 (Amended). A method for modulating the effect on  
cells of the B1 protein of SEQ ID NO:1, comprising applying  
the ribozyme procedure in which a vector encoding a ribozyme  
sequence capable of interacting with a cellular mRNA sequence  
encoding a B1 protein of SEQ ID NO:1 is introduced into said  
cells in a form that permits expression of said ribozyme  
sequence in said cells, and wherein when said ribozyme  
sequence is expressed in said cells it interacts with said  
cellular mRNA sequence and cleaves said mRNA sequence  
resulting in the inhibition of expression of said B1 protein  
in said cells.

Delete claim 20 without prejudice toward the  
continuation of prosecution thereof in a divisional  
application.

Delete claim 21 without prejudice.

AVAILAPL'S CO., INC.

C11 22 (Amended). A pharmaceutical composition for the modulation of the inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by the B1 protein of SEQ ID NO:1 comprising a pharmaceutically acceptable excipient and, as active ingredient, at least one polypeptide according to claim 40.

*mb  
JY* 23 (Amended). A pharmaceutical composition for the modulation of inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by the B1 protein of SEQ ID NO:1, comprising a pharmaceutically acceptable excipient and, as active ingredient, a recombinant animal virus vector encoding a protein capable of binding a cell surface receptor and encoding said polypeptide according to claim 40.

24 (Amended). A pharmaceutical composition for modulating the inflammation, cell death, cell survival or other pathways in cells which are modulated directly or indirectly by the B1 protein of SEQ ID NO:1, comprising a pharmaceutically acceptable excipient and, as active ingredient, an oligonucleotide sequence encoding an antisense sequence of at least part of a mRNA sequence encoding of the B1 protein mRNA sequence, according to claim 40.

Delete claim 25-28 without prejudice toward the continuation of prosecution thereof in a divisional application.

C12 29 (Amended). A method of modulating apoptotic processes or programmed cell death processes (cell death)

C12 pathways) in which the B1 protein of SEQ ID NO:1 is involved directly or indirectly, comprising treating said cells with one or more polypeptide according to claim 40, wherein said treating of said cells comprises introducing into said cells said one or more polypeptide in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the ingestion of said sequence into said cells in a way that said sequence is expressed in said cells.

C13 30 (Amended). A method of modulating cell survival processes in which the B1 protein of SEQ ID NO:1 is involved directly or indirectly and which include the modulation of cell survival, comprising treating said cells with one or more polypeptide according to claim 40, wherein said treating of cells comprises introducing into said cells said one or more polypeptide in a form suitable for intracellular introduction thereof, or introducing into said cells a DNA sequence encoding said one or more polypeptide in the form of a suitable vector carrying said sequence, said vector being capable of effecting the insertion of said sequence into said cells in a way that said sequence is expressed in said cells.

31 (Amended). A method for screening of a ligand capable of binding to a polypeptide according to claim 40, comprising contacting an affinity chromatography matrix to which said polypeptide is attached with a cell extract whereby

C13

the ligand is bound to said matrix, and eluting, isolating, analyzing and producing said ligand.

32 (Amended). A method for screening of a DNA sequence coding for a ligand capable of binding to a polypeptide according to claim 40, comprising applying the yeast two-hybrid procedure in which a sequence encoding said polypeptide is carried by one hybrid vector and sequences from a cDNA or genomic DNA library are carried by the second hybrid vector, transforming yeast host cells with said vectors, isolating the positively transformed cells, extracting said second hybrid vector to obtain a sequence encoding said ligand, and identifying and producing said ligand.

33 (Amended). A method for identifying and producing a ligand capable of modulating the cellular activity modulated or mediated by the B1 protein of SEQ ID NO:1, comprising:

a) screening for a ligand capable of binding to a polypeptide comprising at least a portion of said B1 protein having at least some of the amino acid residues of SEQ ID NO:1, which include essentially all of the prodomain (or CARD) of said B1 protein;

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known proteins having a prodomain (CARD), found by said screening step to be capable of said binding; and

**BEST AVAILABLE COPY**

C13

c) producing said ligand in substantially isolated and purified form.

34 (Amended). A method for identifying and producing a ligand capable of modulating the cellular activity modulated or mediated by a polypeptide according to claim 40, comprising:

a) screening for a ligand capable of binding to a polypeptide comprising at least the carboxy terminal portion of the B1 sequence of SEQ ID NO:1, including the prodomain (CARD);

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known proteins having a prodomain (CARD), found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

35 (Amended). A method for identifying and producing a ligand capable of modulating the cellular activity modulated or mediated by the B1 protein, comprising

a) screening for a ligand capable of binding to at least the N-terminal portion of the B1 sequence of SEQ ID NO:1, including substantially all of the kinase domain of B1;

b) identifying and characterizing a ligand, other than BCL2, TRAF2, or portions of a receptor of the TNF/NGF receptor family or other known intracellular modulatory

BEST AVAILABLE COPY

C13 proteins, found by said screening step to be capable of said binding; and

c) producing said ligand in substantially isolated and purified form.

36 (Amended). A method for identifying and producing a molecule capable of directly or indirectly modulating the cellular activity modulated or mediated by the B1 protein of SEQ ID NO:1, comprising:

a) screening for a molecule capable of modulating activities modulated or mediated by said B1 protein;  
b) identifying and characterizing said molecule; and  
c) producing said molecule in substantially isolated and purified form.

37 (Amended). A method for identifying and producing a molecule capable of directly or indirectly modulating the cellular activity modulated or mediated by a polypeptide according to claim 40, comprising:

a) screening for a molecule capable of modulating activities modulated or mediated by said polypeptide;  
b) identifying and characterizing said molecule; and  
c) producing said molecule in substantially isolated and purified form.

Delete claim 38 without prejudice.

Delete claim 39 without prejudice toward the continuation of prosecution thereof in a continuing application.